The less familiar side of heart failure: Symptomatic diastolic dysfunction

Diastolic heart failure is not as well studied as systolic, but its prevalence has probably been underestimated

Practice recommendations

- Arrange for echocardiography or radionuclide angiography within 72 hours of a heart failure exacerbation. An ejection fraction >50% in the presence of signs and symptoms of heart failure makes the diagnosis of diastolic heart failure probable (B).

- To treat associated hypertension, use angiotensin receptor blockers (ARBs), angiotensin-converting enzyme (ACE) inhibitors, beta-blockers, calcium channel blockers, or diuretics to achieve a blood pressure goal of <130/80 mm Hg (C).

- When using beta-blockers to control heart rate, titrate doses more aggressively than would be done for systolic failure, to reach a goal of 60 to 70 bpm (B).

- Use ACE inhibitors/ARBs to decrease hospitalizations, decrease symptoms, and prevent left ventricular remodeling (A).

Heart failure is a growing epidemic in the US, estimated to cause at least 20% of all hospitalizations in persons over 65 years of age. It is also the leading inpatient diagnosis among Medicare recipients with this age group.1,2,3 More than 5 million people in the US have heart failure, with approximately 550,000 new cases diagnosed annually.

Growing epidemiologic evidence suggests that studies of heart failure have underrepresented a large patient population with a natural history different from that of left ventricular (LV) systolic dysfunction.4-8 One third to one half of patients with signs and symptoms of heart failure have preserved left ventricular function (LVF). They are said to have diastolic heart failure (DHF).

Identifying persons with this less-understood form of heart failure can be challenging. Skillful discernment is needed to avoid mistakenly attributing symptoms to other causes. DHF is particularly common among elderly women with hypertension; every patient with signs and symptoms of heart failure should undergo echocardiography to determine LV function.

Though the evidence base for DHF treatment is less well established than it is for systolic heart failure (SHF), data from recent trials have offered a promising direction.

■ New categorization of heart failure

The relative scopes of DHF and SHF will be better appreciated by understanding
The terms low- vs high-output failure have been replaced in favor of distinguishing between abnormalities of systolic and diastolic function. ACC/AHA Heart Failure Staging System

Severity of heart failure symptoms has traditionally been gauged by the New York Heart Association (NYHA) classification system. A criticism of the NYHA scale, however, is that patients may fluctuate in and out of the varying functional classes. To correct this shortcoming of the NYHA scale, the ACC and the AHA devised a new staging system to describe the progression of heart failure. The premise of this new system is to provide permanence to each sequential progression through the stages of heart failure while complementing the existing NYHA scale.

New model. Patients with Stage A heart failure are at high risk of developing clinical HF and are not representative of any patients categorized under the NYHA functional classification system, as they are not yet symptomatic. Patients with Stage B heart failure have some form of structural heart disease without associated symptoms and correlate best with NYHA Class I patients. Patients with Stage C heart failure have the same underlying structural cardiac disorders associated with Stage B, but they have past or current symptoms of HF. Depending on the severity of their condition, patients with Stage C heart failure may fall within any of the NYHA functional classes. Patients with Stage D heart failure have symptoms refractory to optimized medical and interventional therapies and are representative of NYHA Class IV patients.

### TABLE 1

<table>
<thead>
<tr>
<th>ACC/AHA STAGES OF HEART FAILURE</th>
<th>NYHA FUNCTIONAL CLASSIFICATION</th>
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<tbody>
<tr>
<td>A – high risk for development of HF; no underlying structural cardiac disease (ie, hypertension, diabetes, hyperlipidemia, etc)</td>
<td>No correlation</td>
</tr>
<tr>
<td>B – Structural heart disease but asymptomatic (ie, LVH)</td>
<td>I – patients with no limitation of activities; they suffer no symptoms from ordinary physical activity</td>
</tr>
<tr>
<td>C – Structural heart disease with past or current symptoms of heart failure</td>
<td>II – patients with slight, mild limitation of activity; they are comfortable with rest or with mild exertion</td>
</tr>
<tr>
<td>D – Refractory heart failure</td>
<td>IV – patients who should be at complete rest, confined to bed or chair; any physical activity brings on discomfort and symptoms occur at rest</td>
</tr>
</tbody>
</table>

Patients with Stage A heart failure are at high risk of developing clinical HF and are not representative of any patients categorized under the NYHA functional classification system, as they are not yet symptomatic. Patients with Stage B heart failure have some form of structural heart disease without associated symptoms and correlate best with NYHA Class I patients. Patients with Stage C heart failure have the same underlying structural cardiac disorders associated with Stage B, but they have past or current symptoms of HF. Depending on the severity of their condition, patients with Stage C heart failure may fall within any of the NYHA functional classes. Patients with Stage D heart failure have symptoms refractory to optimized medical and interventional therapies and are representative of NYHA Class IV patients.
Risk factors for the development of DHF include advanced age, female sex, hypertension, and coronary ischemia.

Who is at risk for DHF?
Risk factors for the development of DHF include advanced age, female sex, hypertension, and coronary ischemia. Approximately 50% of those older than 70 years who have heart failure have preserved LV function. In a large epidemiologic

Heart Failure Staging System correlates with the NYHA Classification scheme. Family practitioners can use the new heart failure staging system to identify and recognize risk factors for the development of heart failure and then seek to aggressively prevent or reverse them.

### TABLE 2

<table>
<thead>
<tr>
<th>Characteristics of patients with systolic vs diastolic heart failure</th>
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<tbody>
<tr>
<td><strong>Differentiating systolic and diastolic dysfunction</strong></td>
</tr>
<tr>
<td>Dilated myocardium—classic systolic dysfunction</td>
</tr>
<tr>
<td><strong>Etiology</strong></td>
</tr>
<tr>
<td><strong>Gender-specific differences</strong></td>
</tr>
<tr>
<td><strong>Age-related differences</strong></td>
</tr>
<tr>
<td><strong>Echocardiographic findings</strong></td>
</tr>
<tr>
<td><strong>Symptomatology</strong></td>
</tr>
<tr>
<td><strong>Long-term prognosis</strong></td>
</tr>
</tbody>
</table>

MI, myocardial infarction; LVEF, left ventricular ejection fraction.
Risk factors and preserved LV function support the diagnosis of diastolic heart failure; physical examination is not helpful

Hypertension is a well known cause of left ventricular hypertrophy (LVH), which is a causal mechanism for DHF. Levy et al, in a study of 5143 subjects from the original Framingham Heart Study participants and Framingham Offspring participants, found that hypertension predated the development of heart failure in 91% of cases among patients in this cohort. In this sample, hypertension also carried the greatest population-attributable risk for the development of heart failure of all risk factors considered (39% in men and 59% in women). Hypertension also had the highest prevalence of all risk factors in this study (60% in men and 62% in women). Untreated hypertension leads to an increasing incidence of LVH and associated diastolic dysfunction. Increased LV mass and stiffness cause noncompliance and abnormal relaxation of the ventricular wall leading to increased diastolic pressures.

Coronary ischemia can also cause diastolic dysfunction. Data from the Framingham Heart Study indicate that the prevalence of MI was 10% in hypertensive men and 3% in hypertensive women. MI is a well known precursor of LV systolic dysfunction; however, the relationship to diastolic dysfunction is less clear. Although the prevalence of MI was associated with a 5- to 6-fold risk for heart failure in Framingham subjects, after adjustment for age and other risk factors, fewer than half of the patients who subsequently developed heart failure had a history of MI. This finding supports the role of untreated hypertension in the pathogenesis of DHF.

Physical examination does not help distinguish between DHF and SHF. Signs and symptoms of both disorders are relatively the same. Therefore, the presence of one or more of these risk factors in the setting of heart failure and preserved LV function supports the role of untreated hypertension in the pathogenesis of DHF.

Diagnosis is made clinically

No consensus exists on standardized criteria for diagnosing diastolic heart failure. However, 3 diagnostic levels—possible, probable, and definite DHF—have been proposed by Vasan and Levy.

Possible DHF is defined as signs and symptoms of heart failure (TABLE 3) in patients with normal LV function, but lacking an assessment of ventricular func-
### Managing the patient with possible diastolic heart failure

<table>
<thead>
<tr>
<th>Decision Path</th>
<th>Action</th>
</tr>
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<tbody>
<tr>
<td>Patient exhibits signs/symptoms of heart failure (see Table 3)</td>
<td>Order CBC, CMP, TSH, ECG; cardiac enzymes if warranted; consider BNP if other tests negative or inconclusive</td>
</tr>
<tr>
<td>With an ejection fraction ≤50%, presume a diagnosis of systolic heart failure</td>
<td>Pursue other possible causes of the patient’s symptoms</td>
</tr>
<tr>
<td>Is the ejection fraction ≥50%?</td>
<td>Arrange for echocardiographic examination</td>
</tr>
<tr>
<td>Yes</td>
<td>Give diuretics as required if there is volume overload or active symptoms; titrate carefully to avoid excessive preload reduction</td>
</tr>
<tr>
<td>No</td>
<td>Beta-blocker is indicated to lower heart rate and prolong ventricular relaxation time to improve LV filling. Does the patient also have severe bronchospastic disease?</td>
</tr>
<tr>
<td>Yes</td>
<td>Give ARB or ACE inhibitor to reduce hospitalization, decrease symptoms, and prevent further left ventricular remodeling*</td>
</tr>
<tr>
<td>No</td>
<td>Give aspirin to reduce overall risk of cardiovascular disease</td>
</tr>
<tr>
<td>Titrate beta-blocker to a heart rate of 60 to 70 bpm</td>
<td>Give verapamil or diltiazem instead</td>
</tr>
<tr>
<td>Yes</td>
<td>Give nitrates, as appropriate</td>
</tr>
<tr>
<td>No</td>
<td>Consider giving digoxin</td>
</tr>
<tr>
<td>Does the patient have angina, or do you suspect CAD is present?</td>
<td>Minimize and/or treat other HF risk factors, titrate medication to achieve BP goal &lt;130/80 mm Hg, dietary counseling and modification as appropriate</td>
</tr>
<tr>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Does the patient have refractory tachyarrhythmias?</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td></td>
</tr>
</tbody>
</table>

ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; BNP, b-type natriuretic peptide; CAD, coronary artery disease; CBC, complete blood count; CMP, complete metabolic panel; ECG, electrocardiogram; LV, left ventricular; TSH, thyroid-stimulating hormone.

*The role of concurrent nitrates and hydralazine for ACE inhibitor/ARB-intolerant diastolic heart failure is not well defined and should be employed cautiously.
Elevated BNP—
at least 62 pg/mL—
can help confirm
the diagnosis of
heart failure; small studies have
shown it to be
a valid marker
of DHF.

Probable DHF is defined as (1) signs
and symptoms of heart failure and (2) an
ejection fraction >50% measured via
echocardiography or radionuclide angio-
graphy within 72 hours of the heart failure
exacerbation.

Definite DHF is defined as (1) signs
and symptoms of heart failure, (2) an
ejection fraction >50% measured via
the above methods within 72 hours of the
patient’s presentation, and (3) increased
left-ventricular end diastolic pressure
(LVEDP) measured during cardiac
catheterization.

Direct assessment of diastolic
function unnecessary
Evidence of diastolic dysfunction as
determined by echocardiography or car-
diac catheterization has been debated as
a necessary third diagnostic criterion.24
The problem, though, is that there is no
simple means of reliably diagnosing dias-
tolic dysfunction with echocardiography
(E:A ratios, deceleration or relaxation
times), and that performing cardiac
catheterization to measure LVEDP is
impractical.22

Furthermore, Zile et al have shown
that, though cardiac catheterization helps
to confirm diastolic dysfunction, it is not
necessary to establish the diagnosis. In
this study, 63 patients with clinically
defined diastolic heart failure based on
the Framingham criteria underwent
diagnostic cardiac catheterization; 58
(92%) of these patients were also found
to have an abnormal LVEDP, indicative
of diastolic dysfunction.25 Therefore, the
diagnosis of DHF can be made in the
setting of heart failure in a patient with a
normal ejection fraction.

Order echocardiography
within 72 hours of symptom onset
A major challenge for clinicians is to deter-
mine whether a patient’s dyspnea is a true
symptom of heart failure. Signs and symp-
toms of heart failure must be defined using
clinical indicators such as the Framingham
heart failure criteria (FIGURE).26 Diagnosis
of heart failure is more easily made for a
patient presenting to the emergency depart-
ment with acute pulmonary edema than it is
for an outpatient seen repeatedly for short-
ness of breath over months.

For a patient presenting with acute pul-
monary edema, an echocardiogram should
be performed within 72 hours of symptoms
to document cardiac function in proximity
to the heart failure exacerbation. The ejection
fraction of patients with DHF can
remain within normal range, even during
acute decompensation.27,28 Stroke volume
and cardiac output may be decreased
despite a normal ejection fraction.

Cardiogenic pulmonary edema in
DHF patients results from the stiffened
ventricle’s inability to compensate for
increased venous return due to an expan-
sion in central blood volume or sodium
retention. Subsequently, diastolic pressures
elevate and impede lung compliance,
which increases the work of breathing and
dyspnea.20,29 A normal ejection fraction and
symptom diminishment following diuresis
in the setting of acute decompensation help
confirm the diagnosis of DHF, especially
when other disease states are complicating
the clinical picture.30

Elevated BNP levels may be helpful
An elevated level of b-type natriuretic
peptide (BNP) can help confirm the clini-
cal diagnosis of heart failure, and it has
been shown in small studies to be a valid
marker of DHF.31,32 In a study of 294
patients referred for echocardiography to
evaluate LV function, Lubien et al found
that a BNP value of at least 62 pg/mL had
a sensitivity of 85%, a specificity of 83%,
and an accuracy of 84% for heart failure
in patients with a normal ejection frac-
tion.32 All patients with systolic dysfunc-
tion defined by an ejection fraction <50%
were excluded from this study. These
results, though promising, must be con-
ﬁrmed by further studies evaluating the
diagnostic utility of BNP to detect active
heart failure symptoms in patients with
diastolic dysfunction.
Symptomatic diastolic dysfunction

Treatment should focus on symptom reduction, control of heart rate, balancing fluid status, decreasing ischemia, and achieving blood pressure goals.

**TABLE 4**

Comparative evidence base for evaluation and treatment of systolic vs diastolic heart failure

<table>
<thead>
<tr>
<th>FEATURE</th>
<th>SYSTOLIC HEART FAILURE</th>
<th>DIASTOLIC HEART FAILURE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevalence and risk factors</td>
<td>III</td>
<td>III</td>
</tr>
<tr>
<td>Non-invasive diagnostic methodologies</td>
<td>I – assessment of LVEF</td>
<td>IV, VII†</td>
</tr>
<tr>
<td></td>
<td>I – measurement of BNP levels</td>
<td></td>
</tr>
<tr>
<td>Prognosis</td>
<td>I – II</td>
<td>II, III</td>
</tr>
<tr>
<td>Treatment with ACE inhibitor, ARB, beta-blockers, and digitalis</td>
<td>I†</td>
<td>II, V–VII</td>
</tr>
<tr>
<td>Prevention trials (treatment of asymptomatic precursor condition)</td>
<td>I</td>
<td>None</td>
</tr>
</tbody>
</table>

* I. evidence from several large, well-conducted randomized controlled trials
  II. evidence from a single large, randomized controlled trial or small, well-conducted randomized controlled studies
  III. evidence from well-conducted cohort studies
  IV. evidence from well-conducted case-control studies
  V. evidence from uncontrolled or poorly controlled studies
  VI. conflicting evidence, but tending to favor the recommendation
  VII. expert opinion

† Diagnosis is primarily by exclusion of systolic heart failure; measurement of LVEF and BNP is also useful.
‡ Cochrane review and meta-analysis.

ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; LVEF, left ventricular ejection fraction; BNP, B-type natriuretic peptide.

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**FAST TRACK**

**Treatment of symptomatic diastolic dysfunction**

For SHF patients, multiple large outcome trials have clearly documented the benefit of angiotensin-converting enzyme (ACE) inhibitors, beta-blockers, and aldosterone antagonists in reducing mortality.33–36 The relative paucity of outcome data for DHF has resulted in medical therapy primarily centered on modifying physiologic factors to improve LV filling and relaxation. Specifically, treatment should focus on symptom reduction, balancing fluid status, controlling heart rate, decreasing any ischemia, and achieving blood pressure goals.19,20,22,31 Though many of the medications used to treat SHF are also used for DHF, there are several important differences in appropriate initiation and subsequent titration of these drugs in the 2 settings.20,31

While treatment of DHF is largely theoretical, a limited number of well-designed, randomized studies are available to help determine appropriate therapy.37–39 **TABLE 4** provides a summary of the evidence base for evaluation and treatment of systolic vs diastolic heart failure.40 **TABLE 5** gives a synopsis of these studies. A suggested diagnostic and treatment approach for patients with DHF is outlined in the **FIGURE**. After determining whether a patient has DHF—primarily through the ruling out of other conditions and confirmation with echocardiographic studies—consider the applicability of each treatment based on a patient’s medical history and present condition.

**Medications to control blood pressure**

Hypertension is a major risk factor for DHF, and the ACC/AHA heart failure guidelines recommend a lower blood press-
Guidelines recommend a lower blood pressure goal for patients with DHF than those with uncomplicated hypertension (ie, <130/80 mm Hg). Angiotensin receptor blockers (ARBs), ACE inhibitors, beta-blockers, calcium channel blockers, and diuretics may all be employed to achieve this blood pressure goal.

Angiotensin II receptor blockers. The use of ARBs in the treatment of DHF was recently evaluated in the CHARM-Preserved Study. Candesartan, 32 mg once daily, when added to a background therapy of mostly diuretics and beta-blockers (initially excluding the use of ACE inhibitors but later permitted in appropriate patients following the release of the HOPE trial results), was found to have a modest impact in preventing recurrent admissions for heart failure exacerbations (number needed to treat [NNT]=42 over 3 years). Candesartan also demonstrated a more favorable impact on the composite end-point of cardiovascular death, hospitalization for heart failure, MI, and stroke (NNT=36).

ACE inhibitors. For post-MI patients with DHF, ACE inhibitors have improved treadmill duration and NYHA functional class. Further studies are needed to determine whether an ACE inhibitor or an ARB is preferred or whether they may be used safely together in the management of DHF.

Beta-blockers. Propranolol, when added to an ACE inhibitor and diuretic, has been shown to significantly reduce mortality in a small prospective study of 158 post-MI patients with an average LVEF of 56% and NYHA Class II or III symptoms. Seventy percent of the study patients were women (n=111) and the mean age was 81 years. The dose of propranolol in this study was increased in 10-mg increments at 10-day intervals up to a total daily dose of 30 mg 3 times daily. All 79 patients randomized to receive propranolol successfully reached the target dose; however, 14% (n=11) discontinued therapy due to worsening heart failure or hypotension. The absolute reduction in total

<table>
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<th>TABLE 5</th>
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**Diastolic heart failure outcome trials**

<table>
<thead>
<tr>
<th>TRIAL</th>
<th>BACKGROUND AND CONTEXT</th>
<th>REPRESENTATIVE PATIENT POPULATION</th>
<th>AVG LVEF OF PARTICIPANTS</th>
<th>NNT</th>
<th>SOR* (LOE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHARM-Preserved</td>
<td>Candesartan added to standard heart failure therapy in patients with LVEF &gt;40%</td>
<td>N=3023</td>
<td>60% NYHA Class II</td>
<td>54%</td>
<td>36†</td>
</tr>
<tr>
<td></td>
<td>38% NYHA Class III</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>2% NYHA Class IV</td>
<td></td>
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<tr>
<td>DIG Ancillary Trial</td>
<td>Digoxin + ACE inhibitors and diuretics in patients with LVEF &gt;45%</td>
<td>N=988</td>
<td>NYHA classification not specified</td>
<td>Not reported</td>
<td>N/A†</td>
</tr>
<tr>
<td>Propranolol Study, Aronow et al</td>
<td>Propranolol added to ACE inhibitors and diuretics in post-MI patients with LVEF ≥40%</td>
<td>N=158</td>
<td>52% NYHA Class II</td>
<td>56%</td>
<td>5‡</td>
</tr>
<tr>
<td></td>
<td>48% NYHA Class III</td>
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</table>

*Based on the guidelines for evidence quality outlined by the Center for Evidence-Based Medicine, available at: www.cebm.net/levels_of_evidence.asp. A(1b) = consistent level 1 studies; individual randomized controlled trial (with narrow confidence interval). B(1b) = consistent level 2 or 3 studies or extrapolations from level 1 studies; individual randomized controlled trial (with narrow confidence interval)† For the composite of cardiovascular death, hospital admission for heart failure, MI, or cerebrovascular accident over 3 years‡ For recurrent admissions for heart failure exacerbations over 3 years§ No statistical differences between groups in rates of hospitalization or mortality over 3 years¶ All-cause mortality over a mean of 32 months

NNT, number needed to treat to prevent one death or other specified endpoint; LVEF, left ventricular ejection fraction; ACE, angiotensin-converting enzyme; NYHA, New York Heart Association classification; CHARM, Candesartan in Heart failure: Assessment of Reduction in Mortality and morbidity; DIG, Digitalis Investigation Group.
mortality among patients receiving propranolol was 20%, compared with the study group receiving only standard heart failure therapy (NNT=5 for a median of 32 months of follow-up, \( P=.007 \)). The positive effect of beta-blocker therapy in this small study merits another larger, complementary trial to confirm its benefits in a bigger patient population with the same characteristics.

### Control of volume status

**Diuretics.** It has long been recognized that diuretics are a useful and necessary adjunct in the management of volume overload in patients with heart failure\(^4^2\); however, no large, long-term studies are available to evaluate the effects of these medications on mortality.\(^4^3\) Without concurrent ACE inhibitor/ARB and beta-blocker therapy, diuretics have been shown to cause rebound sympathetic activation.\(^4^4,4^5\)

For patients with either systolic or diastolic dysfunction, diuretics may be dosed aggressively to achieve euvolemia. But for patients with DHF who are partly dependent on volume coupled with increased heart rate to maintain cardiac output, excessive diuresis can cause a significant reduction in preload, which can worsen symptoms.\(^2^0,2^2,3^0\) It is advocated that long-term diuretics should be used judiciously in the treatment of both SHF and DHF, with individualized, tailored therapy being preferred and daily weights used as a guide to determine optimum fluid status.\(^9\)

### Medications to control heart rate

**Beta-blockers.** In addition to their anti-hypertensive effects, beta-blockers may also be used as rate-lowering therapy in the treatment of DHF. Dosing and titration in this setting are handled differently than for SHF. Whereas titration of beta-blockers in SHF requires careful adjustment to avoid worsening of the patients’ symptoms and subsequent exacerbation,\(^4^6-4^8\) dosing in DHF can be more aggressive, with a resting heart rate goal of 60 to 70 bpm.\(^2^0,4^9\) Beta-blockers are used as negative chronotropes in this instance to improve left ventricular filling. Beta-blockers are also useful in the management of ischemia and angina associated with diastolic heart failure.\(^1^9,2^0\)

**Calcium channel blockers.** For patients with contraindications to beta-blocker therapy, non-dihydropyridine calcium channel blockers (verapamil, diltiazem) may be employed as rate-lowering therapy for DHF.\(^1^9\) Unlike the other drugs used in DHF, non-dihydropyridine calcium channel blockers have no role in the treatment of SHF except in the presence of tachyarrhythmias.\(^2^0\)

Dihydropyridine calcium channel blockers (ie, amlodipine, felodipine) may be reserved for heart failure patients in general with angina refractory to beta-blockers. Amlodipine and felodipine are probably the safest of the dihydropyridine calcium channel blockers to use for the treatment of angina as they have not been shown to worsen existing SHF.\(^1^0,5^1\) Verapamil has been shown in a small study to increase exercise capacity and heart failure score in patients with DHF.\(^5^2\)

**Digitalis.** The use of digoxin in patients with DHF was evaluated in the Digitalis Investigation Group (DIG) ancillary trial, a parallel substudy of the overall DIG Trial that enrolled 988 patients with diastolic dysfunction.\(^3^9\) DHF patients receiving digoxin were found to have fewer symptoms and hospitalizations, although this finding was not statistically significant. These findings should be weighed against recent data suggesting that digoxin predisposes women with depressed left ventricular systolic dysfunction to an increased risk of death.\(^5^3\) The role of digoxin in DHF is unclear, and it is recommended that its use be restricted to patients with recurrent hospitalizations and refractory tachyarrhythmias despite optimized medical therapy.\(^9,2^0,3^0,5^4\)

### Prognosis

The annual mortality of patients with DHF has been reported as 5% to 8%, whereas mortality associated with SHF approximates 10% to 15%. However, in patients aged >70 years, both SHF and DHF have a 5-year mortality of 50% and
both have an estimated 50% annual hospital admission rate.54

**Looking forward**

Greater recognition of the disorder and more enrollment of patients with DHF in outcome-based studies will hopefully improve our understanding and approach to treatment of this specific form of heart failure.40,55

Ongoing studies that may provide more evidence-based data to guide therapy for DHF include the Irbesartan in Heart Failure with Preserved Systolic Function Trial (I-PRESERVE), Perindopril for Elderly People with Chronic Heart Failure Study (PEP-CHF) and Study of the Effects of Nebivolol Intervention on Outcomes and Rehospitalisation in Seniors with Heart Failure (SENIORS).56–58

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**CONFLICT OF INTEREST**

The authors of this manuscript have no conflicts of interest in the conception or preparation of this review.

**REFERENCES**


**DRUG BRAND NAMES**

Amlodipine • Norvasc
Candesartan • Atacand
Digoxin • Lanoxin
Diltiazem • Cardizem, Cartia, Placor, Tiazac
Enalapril • Vasotec
Felodipine • Plendil
Hydrazaline • Apresoline
Propanolol • Betachron, Inderal
Verapamil • Calan, Covem, Isoptin, Verelan